burden. Improving the control of PD motor symptoms on patients may contribute to prevent anxiety and HRQoL deterioration in caregivers.

PND4

A COMPREHENSIVE LITERATURE REVIEW OF THE BURDEN OF GAUCHER DISEASE

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OBJECTIVES: Gaucher disease (GD) is an inherited, rare, lysosomal storage disorder caused by a genetic deficiency of glucocerebrosidase. The result is the accumulation of the substrate, glucosylceramide, in the lysosomes of macrophage cells in the liver, spleen, bones, lungs, and other vital tissues. Three subtypes of Gaucher disease are recognized: type 1 (GD1, non-neuropathic), type 2 (GD2, acute neuropathic), and type 3 (GD3, subacute/chronic neuropathic). Clinical manifestations of the disease are multisystemic, clinically heterogeneous and require lifelong management. **METHODS:** To better understand the burden of GD, a comprehensive review of the published literature was conducted. MEDLINE, EMBASE, CENTRAL and "grey" literature sources published in English between January 1990 and February 2013 were searched for relevant publications. **RESULTS:** A total of 97 publications focusing on the epidemiologic, clinical, and socioeconomic burden of GD, treatment options and guidelines were summarized. The standardized incidence and prevalence of GD in the general population varies from 0.30 to 5.80 per 100,000 and 0.33 to 1.75 per 100,000, respectively, and GD1 is the predominant type in most regions. The risk of mortality is highest in GD patients younger than age 5 years and generally increased after age 55; the life expectancy is lower than the general population. Common manifestations of GD such as anemia, thrombocytopenia, splenomegaly, hepatomegaly and bone disease lead to a decreased quality of life. Reported GD comorbidities include Parkinson's disease and cancer. Current treatment options consist of enzyme replacement therapy (ERT, standard of care) and substrate reduction therapy (SRT). ERT is the standard of care, though unmet needs still exist, especially for GD2 and GD3. **CONCLUSIONS:** GD is a rare, chronic disease associated with significant burden to patients and caregivers. While ERT is an effective and well-established treatment for GD patients, several unmet needs exist and further research is needed in this area.

PND5

RESTLESS LEG SYNDROME DETECTION IN HEMODIALYSIS

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OBJECTIVES: Restless leg syndrome (RLS) is a condition with possibly high prevalence in hemodialysis (6-60% according to the literature), and a specific treatment available. Thus it's important to identify it among other conditions present in this population that might confound diagnosis (such as peripheral vascular disease or neuropathies). An approach based on a self-completed screening test will be assessed in this study, along with an estimation of RLS prevalence in hemodialysis. **METHODS:** Patients from two hemodialysis units answered a RLS screening test. Those with a positive screening completed the International Restless Legs Syndrome Study Group Rating Scale (IRLS) that assesses symptom severity. A neurophysiologist performed a clinical interview to confirm the diagnosis, including a supervised administration of the IRLS. **RESULTS:** 164 patients were recruited. Mean age was 65.7 years (range 33-87; Pct25-75: 55.5-77.5), 67% were male and mean time in dialysis was 64.16 months. Self-completed screening test identified 69 possible cases of RLS (42.07%). 44 (26.8%) patients had RLS symptoms according to the self-completed IRLS, and 79% of them were classified as having moderate to severe RLS symptoms. The clinician confirmed just 22 of those cases (13.4% of the total sample), with a demographic profile similar to the sample. The screening test had in this sample a sensitivity of 100%, specificity 66.43% and positive predictive value 31.88%. **CONCLUSIONS:** This study found RLS is a relatively common condition in hemodialysis patients. The screening test showed a high sensitivity to detect RLS, but very low specificity, so the confirmation of an expert neurologist or neurophysiologist is neccesary.

PND6

CEREBROSPINAL FLUID F"-AMYLOID1-42 LEVELS IN THE DIFFERENTIAL DIAGNOSIS OF ALZHEIMER'S DISEASE - SYSTEMATIC REVIEW AND META-ANALYSIS

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OBJECTIVES: The purpose of this study was to carry out systematic review of the literature and meta-analysis to evaluate the diagnostic utility of cerebrospinal fluid (CSF) levels of the 42 amino acid form of amyloid-b (Ab_{1-42}) as a biomarker for differentiating Alzheimer's disease (AD) from non-AD dementia. **METHODS:** Design - Systematic literature review was used to evaluate the effectiveness of the Ab for the diagnosis of Alzheimer's disease. The Scottish Intercollegiate Guidelines Network (SIGN) tool was used by two evaluators to evaluate independently the quality of the 15 studies. Data sources - The literature review covered from October 27, 1946, to October 22, 2013, and searched eight domestic databases including Korea Med and international databases including Ovid-MEDLINE, EMBASE, and Cochrane Library. Eligibility criteria for selecting studies - Primary criteria for inclusion were valid studies on (i) patients with mild cognitive impairment with confirmed or suspected AD and non-AD dementia, and (ii) assessment of Ab_{1-42}levels using appropriate comparative tests. **RESULTS:** A total of 15 studies (15 diagnostic evaluation studies) were identified in which levels of CSF Ab_{1-42} were assessed. Meta-analysis was performed on nine robust studies that compared confirmed AD with healthy individuals (n = 1587), 10 studies that compared AD with non-AD dementias (n = 860), and four studies that compared a-MCI (amnestic mild cognitive impairment) with na-MCI (non-amnestic mild cognitive impairment) subjects (n = 857). Overall, Ab_{1-42}levels were reduced in CSF from AD patients versus healthy controls or non-AD dementia. The effectiveness of this test was evaluated for diagnostic accuracy. Diagnostic accuracy for identifying AD by ELISA was high (pooled sensitivity, 0.772 (95% CI 0.747–0.796); pooled specificity, 0.732 (95% CI 0.699–0.762). **CONCLUSIONS:** Reduced CSF Ab_{1-42} levels are of potential utility in the differential diagnosis of AD versus non-AD dementias and healthy controls.

PND7

PREVALENCE OF CYSTIC FIBROSIS AMONG THE U.S. NATIONAL MEDICAID POPULATION

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OBJECTIVES: Cystic fibrosis (CF) prevalence according to U. S. geographic region as well as patient age, gender and race was examined in the U. S. Medicaid population for patients younger than age 45. **METHODS:** Patients ≤45 years from the Medicaid fee-for-service (FFS) population (2008-2009) were identified using International Classification of Disease 9th Revision Clinical Modification (ICD-9-CM) diagnosis code 277.0x. Patients were required to have continuous Medicaid FFS enrollment in both years and no evidence of managed care enrollment. CF prevalence was stratified by U. S. region, state, age group, gender and race, and was measured by number and percentage of patients in each category. **RESULTS:** A total of 2,142 patients were diagnosed with CF among the Medicaid FFS population under age 45 years in 2008 and 2009. Prevalence was the highest (0.17%) for patients under age 17 years, followed by those age 18-35 (0.14%), and 36-45 years (0.06%). However, some states had the highest CF prevalence in the 18-35 age range (Colorado: 0.92%; North Dakota: 0.50%; Kentucky: 0.54%). CF prevalence by race was also examined with the following results: White (0.17%), Hispanic (0.10%), Asian (0.07%), Black (0.06%) and Native American (0.03%). Male patients had a relatively higher prevalence than female patients (0.14% vs. 0.12%). The highest CF prevalence was observed in Colorado (0.47%), followed by Maryland (0.46%), North Dakota (0.31%), Ohio (0.28%) and Pennsylvania (0.27%). Patients residing in the Midwest U. S. region had the highest prevalence rate (0.15%), compared to the South (0.15%), Northeast (0.12%) and West (0.04%) regions. **CONCLUSIONS:** CF prevalence was the highest in patients age <17 years nationwide, however, certain states showed the highest prevalence among patients age 18 to 35. White and male patients residing in the Midwest U. S. region were found to be at higher risk of a CF diagnosis.

PND8

RISK OF RELAPSE AMONG PROPENSITY SCORE MATCHED MULTIPLE SCLEROSIS PATIENTS RECEIVING NATALIZUMAB OR PLATFORM THERAPY IN THE US

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OBJECTIVES: To examine claims-based relapse rates and time to relapse among multiple sclerosis (MS) patients treated with natalizumab or propensity score matched patients treated with platform therapy (interferon beta/glatiramer acetate) in the US. **METHODS:** The Truven Health MarketScan Research Databases were used to identify adults with a MS (ICD-9-CM code 340) diagnosis treated with natalizumab or platform therapy; the first claim between January 1, 2009 and April 1, 2012 was the index. Patients had to have one year continuous enrollment pre- and post-index and remain on index therapy for 12 months. Patients were excluded if they used a non-index therapy in the pre-index. Natalizumab and platform patients were propensity scored matched using nearest neighbor matching on demographic characteristics, selected comorbid conditions and medications, MS severity (using an adaptation of Kurtzke's Functional System), pre-index relapse and pre-index expenditures. MS-relapse was defined as MS-related inpatient (IP) admission, IV or oral corticosteroid use. Cox Proportional Hazard models were used to evaluate time to relapse, controlling for demographic and pre-index clinical characteristics. **RESULTS:** A total of 897 natalizumab patients met the study criteria, 882 of which were 1: 1 matched to 882 platform therapy patients (mean age 45 years, 70% female) with a standardized difference <10 on all matching measures. Compared to platform patients, natalizumab patients were significantly less likely to have MS-relapse post-index (26.5% vs. 35.5%, p<0.001), with lower post-index rates of MS-related IP admissions (1.0% vs. 2.6%), IV-corticosteroid use (15.6% vs. 19.0%) and oral corticosteroid use (15.4% vs. 23.1%) (all p<0.001). Natalizumab patients also had 25 more relapse-free days (308 vs. 283 days, p<0.001). Post-index MS-relapse risk was lower for natalizumab patients (HR=0.69, p<0.001) after controlling for baseline characteristics. **CONCLUSIONS:** Natalizumab was associated with a significantly lower risk and rate of MS-relapse and had longer time to a MS-relapse compared to platform therapy.

PND9

IMAGE-GUIDED NAVIGATION SYSTEMS (IGNS) IMPROVE ACCURACY OF CATHETER PLACEMENT IN SHUNTED HYDROCEPHALUS PATIENTS

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BACKGROUND: The most common surgical complication associated with shunt placement in Hydrocephalus patients is obstruction causing shunt malfunction. The primary cause of obstruction is incorrect placement of the catheter tip, most notably in the choroid plexus. **OBJECTIVES:** To investigate the clinical and economic value of IGNS use in the accurate placement of catheters in Hydrocephalus patients. **METHODS:** A search of the Embase and PubMed electronic databases was conducted to identify studies evaluating the accuracy, effectiveness, quality-of-life (QOL) and economic aspects of IGNS in patients with Hydrocephalus. No language restrictions were applied. **RESULTS:** We conducted a meta-analysis of studies reporting accuracy of ventricular catheter placement in patients with hydrocephalus undergoing shunt placement with stereotactic IGNS versus freehand technique. The definition of accurate catheter placement was similar in all studies. The meta-analysis showed the odds of achieving an accurate catheter placement for surgeons who utilize IGNS was almost 6 times higher (odds ratio 5.55, 95% CI [2.84, 10.85], P<0.00001) than surgeons who used freehand placement techniques. Furthermore, accurate place-

ment of the catheter tip was associated with fewer shunt failures, as demonstrated in 9 clinical studies investigating accurate catheter placement using the AxiEM™ IGNS (Medtronic Inc). In addition to being costly, studies showed shunt revision surgery was associated with significant morbidity and lower long-term QOL. In a study of 80 paediatric Hydrocephalus patients, investigators found that patients with a history of two or more shunt revision surgeries had a significantly worse QOL ($p<0.02$), as measured by the Hydrocephalus Outcomes Questionnaire (HOQ). **CONCLUSIONS:** The use of IGNS significantly increases the accuracy of ventricular catheter placement compared to freehand techniques in hydrocephalus patients undergoing ventricular shunt insertion. Clinical studies have shown the use of IGNS in shunt placement surgery results in lower shunt failure rates, which improve QOL and lowers the economic impact to payers.

PND10

ASSESSING THE COMPARATIVE OUTCOMES FROM TERIFLUNOMIDE AND DIMETHYL FUMARATE STUDIES IN RELAPSING MS: USE OF "NUMBER NEEDED TO TREAT" ANALYSIS

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OBJECTIVES: Teriflunomide and dimethyl fumarate (DMF), oral therapies for relapsing–remitting multiple sclerosis (RRMS), have demonstrated efficacy in clinical trials. Despite challenges in comparing outcomes across studies, exploratory analyses of treatment effects can be compared informally using relative reductions in a specific endpoint. However, these outcomes do not account for differences in disease severity among study populations or differences on very low event rates. The number needed to treat (NNT) to prevent an event is an important outcome to consider for any comparisons within the field of MS. **METHODS:** NNTs were derived using data from studies with teriflunomide 14 mg (TEMSO, NCT00134563; TOWER, NCT00751881) or DMF (DEFINE, NCT00420212; CONFIRM, NCT00451451) based on inverse of absolute differences between treatment and placebo groups. **RESULTS:** Teriflunomide studies included patients with progressive disease; patients in DEFINE had slightly lower Expanded Disability Status Scale scores. Teriflunomide and DMF significantly reduced risk of relapse (all studies). NNTs to prevent one relapse were similar across studies (5.9 [TEMSO], 5.6 [TOWER], 5.3 [DEFINE], 5.6 [CONFIRM]). Risk of disability progression sustained for 12 weeks was significantly reduced in TEMSO, TOWER, and DEFINE but not CONFIRM. Corresponding NNTs to prevent disability progression were 13.8, 17.4, 10.8, and 30.2. Risk of relapse leading to hospitalization was significantly reduced in TEMSO and TOWER but not in DEFINE and CONFIRM. Corresponding NNTs were lower in TEMSO (12.5) and TOWER (20) than in DEFINE (50) and CONFIRM (50). **CONCLUSIONS:** Using the NNT approach, we demonstrate a comparable effect size for teriflunomide and DMF on relapse. NNTs to prevent disability progression with teriflunomide showed a consistent significant reduction in risk versus placebo in both TEMSO and TOWER, whereas for DMF, comparable NNTs were observed only in DEFINE, and not in CONFIRM. Reduction of risk for relapse leading to hospitalization was significant only for teriflunomide.

PND11

THE CLINICAL EVIDENCE BASE OF TREATMENT OPTIONS IN ALZHEIMER'S DISEASE: A SYSTEMATIC LITERATURE SEARCH

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OBJECTIVES: Alzheimer's Disease (AD) destroys brain cells, causing problems with memory, thinking, and behavior severe enough to affect work, family and social relationships, and basic activities of daily living. AD gets worse over time, it is incurable and fatal. Donepezil, galantamine, rivastigmine and memantine are the current treatment options but the latest evidence was not systematically reviewed recently. **METHODS:** PubMed, Health Technology Assessment Database, NHS Economic Evaluation Database, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, DAHTA-Datenbank, PSYNDEX and PsycINFOwere searched systematically for randomized-controlled studies. For the abstracts that met the pre-defined inclusion criteria, full text articles were obtained. The abstracts that did not meet the search criteria were excluded. Based on these manuscripts it was evaluated whether each study meets the selection criteria. **RESULTS:** After elimination of duplicates the search indicated above yielded 418 articles of which another 299 were excluded based on the title selection; after abstract review, 82 articles have been reviewed in full text which were also deemed to be relevant based on the research question. For donepezil 24 RCTs were available for which another 4 subgroup and exploratory analyses have been published. For galantamine 11 RCTs with 6 exploratory analysis are available. For rivastigmine 10 RCTs are available with 7 exploratory papers. For memantine 14 RCTs with 6 exploratory analysis were found. Out of those studies eleven head-to-head studies are available; 5 studies comparing donepezil vs memantine, 3 studies comparing donepezil vs rivastigmine and one study each comparing donepezil vs galatamine, rivastagmine vs memantine. There was one study comparing rivastagmine vs donepezil vs galantamine. In comparison the clinical evidence seems diverse dependent on the patient characteristics, study duration, and severity of disease. **CONCLUSIONS:** Appropriate evidence assessment for the approved AD treatments requires clinical expertise and close review of the study characteristics.

PND12

EVALUATION OF DISABILITY PROGRESSION AS AN ENDPOINT IN CLINICAL TRIALS FOR RELAPSING-REMITTING MULTIPLE SCLEROSIS (RRMS): COMPARISON OF THE DEFINE AND CONFIRM STUDIES

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OBJECTIVES: Time to 12-week confirmed disability progression, measured by the Expanded Disability Status Scale (EDSS), is a key endpoint in RRMS trials. However, the EDSS has widely discussed limitations, and several therapies have shown inconsistent results for this endpoint in terms of statistical significance. Here we contextualize differences in 12-week confirmed disability progression results in the Phase 3 studies of gastro-resistant dimethyl fumarate (DMF), DEFINE and CONFIRM. **METHODS:** Time to 12-week confirmed disability progression at 2 years was a secondary endpoint in both studies; however, the studies were not powered to detect statistical significance for this endpoint. Patients had the option of discontinuing study treatment and initiating alternative therapy at any time due to 12-week confirmed disability progression or after completing 48 weeks of study treatment and experiencing one confirmed relapse after 24 weeks (DEFINE) or two confirmed relapses at any time (CONFIRM). **RESULTS:** Although gastro-resistant DMF 240mg BID demonstrated consistent reductions on 12-week confirmed disability progression, statistical significance was achieved in DEFINE ($p=0.0050$) but not CONFIRM ($p=0.2536$). There was an apparent difference in the placebo rate of 12-week confirmed disability progression at 2 years (DEFINE, 27%; CONFIRM, 17%). In CONFIRM, a relatively higher percentage of placebo patients (4.1%) versus gastro-resistant DMF patients (1.7%) switched to alternative MS therapy or withdrew after the time of tentative disability progression without a subsequent EDSS assessment. Additionally, a relatively higher percentage of placebo patients who switched to alternative MS therapy had ≥2 relapses without 12-week confirmed disability progression prior to switch in CONFIRM (45%) compared with DEFINE (16%). **CONCLUSIONS:** Relapse-based criteria for switching to alternative therapy may have contributed to the lower placebo progression rate and decreased assay sensitivity for this particular endpoint in CONFIRM. The totality of evidence needs to be taken into account when assessing a therapy's effect on disability progression.

PND13

A REAL-WORLD ASSESSMENT OF ANNUAL MULTIPLE SCLEROSIS PREVALENCE AND DISEASE-MODIFYING DRUG TREATMENT RATES USING AN ADMINISTRATIVE CLAIMS DATABASE

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OBJECTIVES: To examine annual prevalence and treatment rates of multiple sclerosis (MS) patients using a large US commercial administrative claims database. **METHODS:** Random sample of 5 million lives from the IMS LifeLink Plus database was used for this analysis. Individuals with ≥1 month eligibility were included in the denominator; those with ≥1 month eligibility and an MS diagnosis (ICD-9-CM: 340. xx) were included in the numerator. Presence of a disease-modifying drug (DMD) was defined as ≥1 claim during the calendar year of interest. Baseline demographics and clinical characteristics were evaluated for each group. Annual prevalence (per 10,000) and treatment rates were reported for each calendar year (2006–2012) and were further stratified by age and gender. **RESULTS:** MS patients were older than patients without MS (mean age range 46.8–47.7 vs. 34.4-35.1, respectively) and more likely to be female (73% vs. 51%, respectively). Comorbidities such as gastrointestinal disorders (42.8%), hypertension (43.5%), arthritis (24.8%) and anxiety (22.8%) were common among MS patients (2006 estimates). MS prevalence ranged from 16.4/10,000 (2006) to 17.8/10,000 (2010). Similar patterns over the years were observed when data were stratified by sex and age, with absolute rates being higher among women vs. men (24.4/10,000 vs. 8.2/10,000, respectively; 2012; $P<0.001$) and patients aged 45–64 years (29.4/10,000 vs. 0.4/, 15.6/ and 18.2/10,000 patients aged <18, 18–44 and ≥65, respectively; $P<0.001$). The proportion of MS patients receiving a DMD increased from 2006 (42.5%) to 2012 (51.2%) ($P<0.001$). Similar rates and trends in the proportion of patients with a DMD were observed when stratified by gender (42.8% (2006) and 51.3% (2012) [female]; 41.5% (2006) and 50.7% (2012) [male]; both $P<0.001$). **CONCLUSIONS:** In a recent 5-year period, MS prevalence in a large US insured population increased slightly, with a greater increase in the likelihood of DMD use.

PND14

THE CHARACTERISTICS OF MULTIPLE SCLEROSIS IN IRAN

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OBJECTIVES: Multiple Sclerosis (MS) is a chronic disease of the Central Nerve System. The aim of this paper is to characterize the various clinical and demographical feature of the MS population. **METHODS:** In a 6-month cross-sectional study248 patients were investigated in Khorasan provinces. Data was collected by employing a 32- item self-administered questionnaire in a face to face interview. **RESULTS:** A total of 248 patients were recruited (186 female, 75%; 62 male, 25%). The mean age was 31.9±8.7, the mean onset age was 26.3 (26.3±8: 1) and the median duration of illness was 3.8 years. The prevalence and incidence were estimated to be 25/100000 and 2.5/100,000 respectively. Significantly more patients had a Relapsing Remitting MS course. Self reported character of MS individuals were significantly more (193, 77.8%) regarding nervous character (p value=.000). A family history of ms was reported in 11%. However, there was no a significant difference between men and women with respect to age, age of onset, BMI, disease duration and gap between clinical onset and diagnosis. The education level was reported as 154 (62%) had a bachelor and greater degree and 94 (38%) had a diploma or under-diploma degree. Thirty six percents of the patients were born in the spring. **CONCLUSIONS:** In contrast to reports from Caucasians, the Iranian differs with respect to age, age of onset of illness, disease duration, family history, sex ratio. The sex ratio of 3: 1 in this study is somewhat higher than the usual 2: 1 in the standard text and seen in Asia or the neighboring Arab countries. This might reflect the role of hormone or genetic factors or much more visiting by women, or women stressful life. These included BMI, birth season, education stand. The educated people in developing country are probably likely to adopt a "western" lifestyle, therefore more probably to get the risk of developing Western disease.